REMARKS

Claims 1-22 are pending; claims 3-4 and 11-13 stand withdrawn. Claims 1, 17, and 19-22 have been amended. Support for the amendments can be found throughout the specification, for example, at 41-42 and 135-137. No new matter has been added.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 2, 5-10, and 14-22 have been rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement. The Examiner argues that claim 1 provides that Y is $-CH_2-$, but "this value is not present in the specification," and that "the applicants have added hydrogen for the value of variable R3 which is not present in the specification." Office Action at 2. Applicants respectfully disagree.

The specification describes that, in some embodiments, Y is $-CH_2-$ on page 23, lines 13-14. At page 16, lines 6-32, the substituents of R_3 are discussed. At lines 22-30, the specification describes that R_3 can be amino acid side chains selected from, among others, glycine. The side chain of the amino acid glycine is hydrogen, as is well known in the art. Accordingly, the specification provides a written description of all features of the compound of claim 1, including Y being $-CH_2-$ and R_3 being hydrogen. Applicants therefore respectfully ask the Examiner to reconsider and withdraw the rejection for lack of written description.

Claims 1, 2, 5-10, and 14-22 have also been rejected under § 112, first paragraph, for lack of enablement. With regard to pharmaceutically acceptable derivatives, the Examiner argues that the specification provides "no teaching or guidance . . . for preparing any specific derivative such as esters, prodrugs, metabolites and residues." Office Action at 3. Claim 1 has been amended to recite "pharmaceutically acceptable salts".

The Examiner also argues that because VLA4 "is only one of several known integrins involved in cell adhesion . . . the instant compounds will have utility in inhibiting cell adhesion mediated by VLA4 alone and furthermore for treating but not preventing or completely inhibiting cell adhesion," (Office Action at 4). This argument is not applicable to claim 1 or the claims that depend from it, as claim 1 is directed to compounds of formula (I). Enablement of claim 1 does not that inhibition, prevention, or suppression of cell adhesion be enabled. The

Examiner does not argue that the specification fails to teach a person of ordinary skill in the art how to make and use the compounds of formula (I).

Claim 17 is directed to a pharmaceutical composition including a compound of claim 1 in an amount effective suppression of **VLA-4 mediated** cell adhesion. Claims 19-21 have been amended similarly to be directed to methods of suppression of **VLA-4 mediated** cell adhesion in a mammal. Claim 22 has also been amended. Applicants respectfully disagree with the Examiner's comment that "[t]here are no working examples present showing efficacy of instant compounds in known animal models of autoimmune diseases, psoriasis, inflammatory diseases and diabetes." See the specification at 141-143, describing use of the compounds in mouse contact hypersensitivity and sheep allergic response to *Ascaris* antigen. From the supposed lack of working examples, the Examiner arrives at the conclusion that "it would require undue experimentation to demonstrate efficacy of instant compounds in known animal models." However, in addition to the working examples mentioned, the specification also teaches that "in vivo experiments suggest that . . . inhibition of VLA-4-dependent cell adhesion may prevent or inhibit several inflammatory and autoimmune pathologies." (specification at 3). The Examiner does not dispute that the compounds can inhibit VLA-4-dependent cell adhesion.

Applicants respectfully ask that the rejections under § 112, first paragraph be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1, 2, 5-10, and 14-22 have been rejected under § 112, second paragraph, as being indefinite, specifically because claim 1 fails to define R_2 and provides two different definitions of R_4. Claim 1 has been amended to correct typographical errors. Applicants believe these amendments address the Examiner's concerns, and respectfully ask that the rejection under § 112, second paragraph be reconsidered and withdrawn.

Double Patenting Rejections

Claims 1, 2, 5-10 and 14-22 have been rejected over:

- claims 1-48 of U.S. Patent No. 6,376,538;
- claims 1-38 of U.S. Patent No. 6,306,804;
- claims 1-20 of U.S. Patent No. 6,552,216;

- claims 1-53 of U.S. Patent No. 6,630,512;
- claims 1-34 of U.S. Patent No. 6,624,152; and
- claims 1-9 of U.S. Patent No. 7,001,921.

A terminal disclaimer under 37 C.F.R. § 1.321(c) is being filed with this reply to obviate the double patenting rejections over each of U.S. Patent No. 6,376,538; U.S. Patent No. 6,306,804; U.S. Patent No. 6,552,216; U.S. Patent No. 6,630,512; U.S. Patent No. 6,624,152; and U.S. Patent No. 7,001,921. In view of the terminal disclaimer being filed with this reply, Applicants respectfully request that double patenting rejections be reconsidered and withdrawn.

CONCLUSION

Applicants ask that all claims be allowed. Please apply any charges or credits to Deposit Account No. 19-4293.

Respectfully submitted,

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